The Examiner also objects to the title of the invention, stating that it is not descriptive of the elected invention. The Examiner requests the instant invention be re-titled.

Applicants respond by respectfully requesting the title of the invention be modified to read:

"Non-invasive methods for detecting non-host DNA in a host using epigenetic differences between the host and non-host DNA."

IN THE CLAIMS:

LISTING OF CLAIMS

(Original) 1. A method for differentiating DNA species originating from different individuals in a biological sample comprising the step of determining epigenetic differences between these DNA species.

(Original) 2. A method according to claim 1 wherein the epigenetic difference is a difference in DNA methylation.

(Original) 3. A method according to claim 1 wherein the biological sample is plasma or serum.

(Original) 4. A method according to claim 1 wherein the biological sample is blood.

(Original) 5. A method according to claim 1 wherein one of the individuals is a pregnant female and the other individual is an unborn fetus.

(Original) 6. A method according to claim 1 wherein one of the individuals is a transplantation recipient and the other individual is an organ donor.

(Original) 7. A method according to claim 6 wherein the transplantation is a bone marrow transplantation.

(Original) 8. A method according to claim 1 further comprising the step of measuring concentrations of DNA species having an epigenetic difference.

(Withdrawn) 9. A method according to claim 2 wherein the epigenetic difference is a DNA methylation difference.

(Original) 10. A method according to claim 2 further comprising the step of adding sodium bisulfite to the biological sample or to the DNA species to detect a DNA methylation difference.

(Original) 11. A method according to claim 2 further comprising the step of performing a methylation-specific polymerase chain reaction to detect a DNA methylation difference.

(Original) 12. A method according to claim 10 further comprising the step of sequencing DNA to detect a DNA methylation difference.

(Original) 13. A method according to claim 10 further comprising the step of performing primer extension to detect a DNA methylation difference.

(Original) 14. A method according to claim 5 wherein the biological sample is maternal plasma or serum.

(Original) 15. A method according to claim 14 further comprising the step of measuring the concentration of fetal DNA in maternal plasma or serum.

(Original) 16. A method according to claim 15 wherein the concentration of fetal DNA measured is used to predict, monitor or diagnose or prognosticate a disorder.

(Amended) 17. A method according to claim ~~1~~5 wherein an epigenetic mark is associated with a fetal or maternal disorder.

(Original) 18. A method according to claim 17 wherein the disorder is a chromosomal aneuploidy.

(Original) 19. A method according to claim 18 wherein the chromosomal aneuploidy is trisomy 21 (Down syndrome).

(Original) 20. A method according to claim 17 wherein the disorder is preeclampsia.

(Original) 21. A method according to claim 17 wherein the disorder is an imprinting disorder.

(Original) 22. A method according to claim 21 wherein the disorder is Prader-Willi syndrome.

(Original) 23. A method according to claim 21 wherein the disorder is Angelman syndrome.

(Original) 24. A method according to claim 14 wherein an epigenetic difference in fetal cells in the placenta is used as a fetus-specific marker in maternal plasma or serum.

(Original) 25. A method according to claim 6 further comprising the step of measuring the concentrations of donor and recipient DNA.

(Original) 26. A method according to claim 25 wherein the measurements are used to predict the clinical progress of the transplantation recipient.

(Original) 27. A method according to claim 1 wherein one individual is male and the other individual is female.

(Original) 28. A method according to claim 27 wherein the epigenetic marker is an inactivated X chromosome of the female individual.

(Original) 29. A method according to claim 28 wherein methylated DNA sequences on the inactivated X chromosome are used to detect DNA originating from the female individual.

(Original) 30. A method according to claim 1 wherein the epigenetic differences are analyzed inside cells.

(Original) 31. A method according to claim 30 wherein the epigenetic differences are analyzed using in-situ methylation-specific polymerase chain reaction.

(Original) 32. A method according to claim 1 wherein the epigenetic differences are used to sort or isolate cells from the individuals.

(Original) 33. A method according to claim 1 wherein the epigenetic differences are used to purify DNA from the individuals.